

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

Claim 1 (Original): 1. A fusion protein with the formula :

(a) X-Y, or

(b) Y-X,

wherein X represents a first immunoregulatory polypeptide;

Y represents a second immunoregulatory polypeptide; and

X is different from Y.

Claim 2 (Original): The fusion protein of claim 1, wherein said X and Y each represents a cytokine.

Claim 3 (Original): The fusion protein of claim 2, wherein X represents a cytokine capable of enhancing a nonspecific immune response.

Claim 4 (Original): The fusion protein of claim 3, wherein said nonspecific immune response is mediated by one or more of the effector cells selected from the group consisting of macrophages, dendritic cells, NK cells and NKT cells.

Claim 5 (Currently Amended): The fusion protein of ~~any one of claims~~ ~~claim 2 to 4~~ claim 2, wherein Y represents a cytokine capable of enhancing a specific immunity.

Claim 6 (Original): The fusion protein of claim 5, wherein said specific immunity is mediated by the effector cells B and/or T lymphocytes.

Claim 7 (Currently Amended): The fusion protein of ~~any one of claim 2 to 6~~ claim 2, wherein X and Y independently are IL-2, IL-7, IL-15, IL-18, IL-21, IL-27, IL-31 or IFN $\gamma$ .

Claim 8 (Original): The fusion protein of claim 7, wherein :

- (a) X is IL-2 and Y is selected from the group consisting of IL-7, IL-15, IL-18, IL-21, IL-27, IL-31 and IFN $\gamma$ ;
- (b) X is IL-12 and Y is selected from the group consisting of IL-15, IL-18 and IL-21;
- (c) X is IL-15 and Y is IL-7, IL-18 or IL-21; or
- (d) X is IL-18 and Y is IL-21.

Claim 9 (Original): The fusion protein of claim 8, which :

- (a) has the formula Y-X, wherein X is IL-2 and Y is IL-7;
- (b) has the formula X-Y or Y-X, wherein X is IL-2 and Y is IL-15 ;
- (c) has the formula X-Y, wherein X is IL-2 and Y is IL-18 ;
- (d) has the formula Y-X, wherein X is IL-2 and Y is IL-21 ;
- (e) has the formula Y-X, wherein X is IL-2 and Y is IFN-g ;
- (f) has the formula X-Y, wherein X is IL-15 and Y is IL-7;
- (g) has the formula X-Y or Y-X, wherein X is IL-15 and Y is IL-18 ;
- (h) has the formula X-Y or Y-X, wherein X is IL-15 and Y is IL-21 ; and
- (i) has the formula X-Y or Y-X, wherein X is IL-18 and Y is IL-21.

Claim 10 (Currently Amended): The fusion protein of ~~any one of claims 7 to 9~~ claim 7, wherein said IL-2 is an IL-2 variant which exhibits a reduced cytotoxicity as compared to the corresponding native IL-2.

Claim 11 (Original): The fusion protein of claim 10, wherein said IL-2 variant is selected from the group consisting of :

- (a) the variant F42K having the phenyl alanine residue in position 42 of the native IL-2 substituted by a lysine residue;
- (b) the variant R38A having the arginine residue in position 38 of the native IL-2 substituted by an alanine residue;
- (c) the variant D20I having the aspartic acid residue in position 20 of the native IL-2 substituted by an isoleucine residue;
- (d) the variant N88G having the asparagine residue in position 88 of the native IL-2 substituted by a glycine residue;
- (e) the variant N88R having the asparagine residue in position 88 of the native IL-2 substituted by an arginine residue;
- (f) the variant Q126M having the glutamine residue in position 126 of the native IL-2 substituted by a methionine residue; and
- (g) any combination of (a) to (f).

Claim 12 (Currently Amended): The fusion protein of ~~any one of claims 7 to 11~~ claim 7, wherein said IL-18 is an IL-18 variant.

Claim 13 (Original): The fusion protein of claim 12, wherein said IL-18 variant is the variant K89A having the lysine residue in position 89 of the corresponding native IL-18 substituted by an alanine residue.

Claim 14 (Currently Amended): The fusion protein of ~~any one of claims 7 to 13~~ claim 7, wherein said IL-18 is a proIL-18.

Claim 15 (Currently Amended): The fusion protein of ~~any one of claims 7 to 14~~ claim 7, wherein said fusion protein comprises an amino acid sequence which is at least 70% homologous to all or part of any of the amino acid sequences recited in SEQ ID NO: 1-19.

Claim 16 (Original): The fusion protein of claim 15, wherein said fusion protein comprises an amino acid sequence which is 100% homologous to all or part of any of the amino acid sequences recited in SEQ ID NO: 1-19.

Claim 17 (Currently Amended): A nucleic acid molecule encoding the fusion protein of ~~any one of claims 1 to 16~~ claim 1.

Claim 18 (Original): A vector containing the nucleic acid molecule of claim 17.

Claim 19 (Original): The vector of claim 18, wherein said vector is derived from one or more bacterial plasmids, bacteriophages, yeast episomes, artificial

chromosomes, or from viruses selected from the group consisting of baculoviruses, papovaviruses, herpes viruses, adenoviruses, adenovirus-associated viruses (AAV), poxviruses, foamy viruses, and retroviruses.

Claim 20 (Original): The vector of claim 19, wherein said vector is an adenoviral vector.

Claim 21 (Original): The vector of claim 20, wherein said vector is an E1- and E3-deleted replication-defective adenoviral vector comprising the nucleic acid molecule according to claim 17 inserted in replacement of the E1 region and placed under the control of the CMV promoter.

Claim 22 (Currently Amended): The vector of ~~any one of claims 18 to 21~~ claim 18, wherein said vector further comprises one or more transgenes encoding (i) a tumor proliferation inhibitor and/or (ii) at least one antigen against which an immune response is desired.

Claim 23 (Original): The vector of claim 22, wherein said tumor proliferation inhibitor is a fusion protein which encodes a two domain enzyme possessing both CDase and UPRTase activities.

Claim 24 (Original): The vector of claim 22, wherein said specific antigen is a HPV antigen selected from the group consisting of E5, E6, E7, L1, and L2 either individually or in combination.

Claim 25 (Original): The vector of claim 24, wherein said HPV antigen is a membrane-anchored form of a non-oncogenic variant of the early HPV-16 E6 and/or E7 antigen.

Claim 26 (Currently Amended): An infectious viral particle comprising a nucleic acid molecule according to claim 17 ~~or a vector according to any of claims 18 to 25.~~

Claim 27 (Original): A process for producing an infectious viral particle ~~according to claim 26,~~ comprising the steps of :

(a) introducing the viral vector of ~~any one of claims 18 to 25~~ claim 18 into a suitable cell line,

(b) culturing said cell line under suitable conditions so as to allow the production of said infectious viral particle, and

(c) recovering the produced infectious viral particle from the culture of said cell line, and

(d) optionally purifying said recovered infectious viral particle.

Claim 28 (Currently Amended): A host cell comprising the nucleic acid molecule according to claim 17 ~~or the vector according to any one of claims 18 to 25 or the infectious viral particle of claim 26.~~

Claim 29 (Currently Amended): A method for producing ~~the~~ a fusion protein according to ~~any one of claims 1 to 16~~, comprising introducing a vector according to ~~any one of claims 18 to 25 or an infectious viral particle according to claim 26~~ claim 18 into a suitable host cell to produce a transfected or infected host cell, culturing *in-vitro* said transfected or infected host cell under conditions suitable for growth of the host cell, and thereafter recovering said fusion protein from said culture, and optionally, purifying said recovered fusion protein.

Claim 30 (Currently Amended): A pharmaceutical composition comprising an effective amount of the fusion protein according to claim 1 ~~any one of claims 1 to 16~~, ~~the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or any combination thereof~~ and optionally a pharmaceutically acceptable vehicle.

Claim 31 (Currently Amended): ~~Use of the fusion protein according to any one of claims 1 to 16, the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or the composition of claim 30,~~ A method for the preparation of a drug intended for treating or preventing cancer or an infectious disease comprising using the fusion protein according to claim 1.

Claim 32 (Currently Amended): The use method according to claim 31, wherein said composition is administered into or in close proximity to a solid tumor.



Claim 33 (Currently Amended): The use method according to claim 31 ~~or 32~~, wherein said fusion protein, said vector, said infectious viral particle, said host cell or said composition is administered in combination with one or more transgenes or transgene products.

Claim 34 (Currently Amended): A method for the treatment of a human or animal organism, comprising administering to said organism a therapeutically effective amount of the fusion protein according to ~~any one of claims 1 to 16, the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or the composition of claim 30~~ claim 1.

Claim 35 (Currently Amended): A method for enhancing an immune response in an animal or human organism comprising introducing into said organism the fusion protein according to ~~any one of claims 1 to 16, the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or the composition of claim 30~~ claim 1, so as to enhance said immune response.

Claim 36 (Currently Amended): ~~Use of the fusion protein according to any one of claims 1 to 16, the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or the composition of claim 30,~~ A method for the preparation of a drug intended for the

purpose of activating maturation of dendritic cells in an animal or human organism comprising using the fusion protein according to claim 1.

Claim 37 (Currently Amended): The use method according to claim 36, wherein the fusion protein has the formula X-Y, wherein X is IL-2 and Y is IL-18 or the formula Y-X, wherein X is IL-2 and Y is IL-7.

Claim 38 (Currently Amended): ~~Use of the fusion protein according to any one of claims 1 to 16, the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or the composition of claim 30, A method~~ for the preparation of a drug intended for the purpose of activating NKT cells in an animal or human organism comprising using the fusion protein according to claim 1.

Claim 39 (Currently Amended): The use method according to claim 38, wherein the fusion protein has the formula X-Y, wherein X is IL-2 and Y is IL-18.

Claim 40 (Currently Amended): ~~Use of the fusion protein according to any one of claims 1 to 16, the vector according to any one of claims 18 to 25, the infectious viral particle according to claim 26, the host cell according to claim 28 or the composition of claim 30, A method~~ for the preparation of a drug providing lower cytotoxicity upon administration in an animal or human organism as compared to the cytotoxicity observed upon administration of the individual X and/or Y entities comprising using the fusion protein according to claim 1.

Claim 41 (Original): The use method according to claim 40, wherein the fusion protein has the formula X-Y, wherein X is IL-2 and Y is IL-18, or the formula Y-X, wherein X is IL-2 and Y is IL-7.

Claim 42 (New): An infectious viral particle comprising a vector according to claim 18.

Claim 43 (New): A host cell comprising the vector of claim 26.

Claim 44 (New): A host cell comprising the infectious viral particle of claim 26.

Claim 45 (New): A pharmaceutical composition comprising an effective amount of the vector according to claim 18.

Claim 46 (New): A pharmaceutical composition comprising an effective amount of the infectious viral particle according to claim 26.

Claim 47 (New): A pharmaceutical composition comprising an effective amount of the host cell according to claim 28.

Claim 48 (New): A method for the treatment of a human or animal organism, comprising administering to said organism a therapeutically effective amount of the vector according to claim 18.

Claim 49 (New): A method for the treatment of a human or animal organism, comprising administering to said organism a therapeutically effective amount of the infectious viral particle according to claim 26.

Claim 50 (New): A method for the treatment of a human or animal organism, comprising administering to said organism a therapeutically effective amount of the host cell according to claim 28.

Claim 51 (New): A method for enhancing an immune response in an animal or human organism comprising introducing into said organism the fusion protein according to the vector according to claim 18, so as to enhance said immune response.

Claim 52 (New): A method for enhancing an immune response in an animal or human organism comprising introducing into said organism the fusion protein according to the infectious viral particle according to claim 26, so as to enhance said immune response.

Claim 53 (New): A method for enhancing an immune response in an animal or human organism comprising introducing into said organism the fusion protein according to the host cell according to claim 28, so as to enhance said immune response.